

REMARKS

Claims 9 and 11 are pending in the application. Claims 10, 12, and 13 have been previously withdrawn from consideration. Claims 1-8 have been previously cancelled. Claim 11 has been previously amended to correct a typographical error. No amendment is made to the pending claims.

The Examiner has maintained the rejection of claims 9 and 11 under 35 U.S.C. § 103(a) over Weder et al. (EP 733372 or its equivalent US 5726164). The Examiner states that one of ordinary skill would have known such orally administrable formulation. Applicants respectfully disagree and request that the rejection be withdrawn.

1. Weder et al pertains to a composition for the intravenous administration of a staurosporin derivative. Weder et al merely teaches that staurosporin derivatives are sparingly soluble in water. (Col 1 ln 1-3; Col 2, ln 30-33). Further, Weder et al teaches that oral absorption is more difficult than intravenously administration for sparingly soluble agents:

"Some therapeutic agents which would be insufficiently capable of oral absorption, can only be administrated by the intravenous route. Other therapeutic agents can be administrated intravenously in a less efficacious dose than is required for oral administration." (Col 1 ln 57-62).

Hence, Weder et al teaches away from the claimed invention. After making reference, the skilled person in the art has no motivation to make the oral formulation of staurosporin derivatives.

2. The claimed invention provided superior unexpected activity.

Weder et al does not teach or suggest oral formulations of staurosporine derivatives.

Henry et al (referred to by the Office Action as known in the art) teaches that the highest plasma concentrations ( $C_{max}$ ) are 0.36 and 0.45  $\mu\text{mol/l}$  at 3<sup>rd</sup> hour ( $t_{max}$ ) for an oral dosage of 100mg of N-benzoylstaurosporine (see, example 3, col 3). In contrast, most of the formulations of the claimed invention provide a  $C_{max}$  of plasma concentration of 0.486-1.212  $\mu\text{mol/l}$  with most  $t_{max}$  about 2nd hour for a only 50mg dosage (Table 2)\*. Such superior effect can not be expected from the Weder disclosure.

\*: Formulation B has a  $C_{max}$  of 0.299  $\mu\text{mol/l}$ .

Therefore, the present inventions are not obvious over Weder et al.


CONCLUSION

The Applicants believe that the Application is now in condition for allowance and request early notice to that effect.

If it will advance prosecution of the Application the Examiner is urged to contact the Applicants' undersigned counsel at the telephone number listed below.

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Respectfully submitted,

  
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